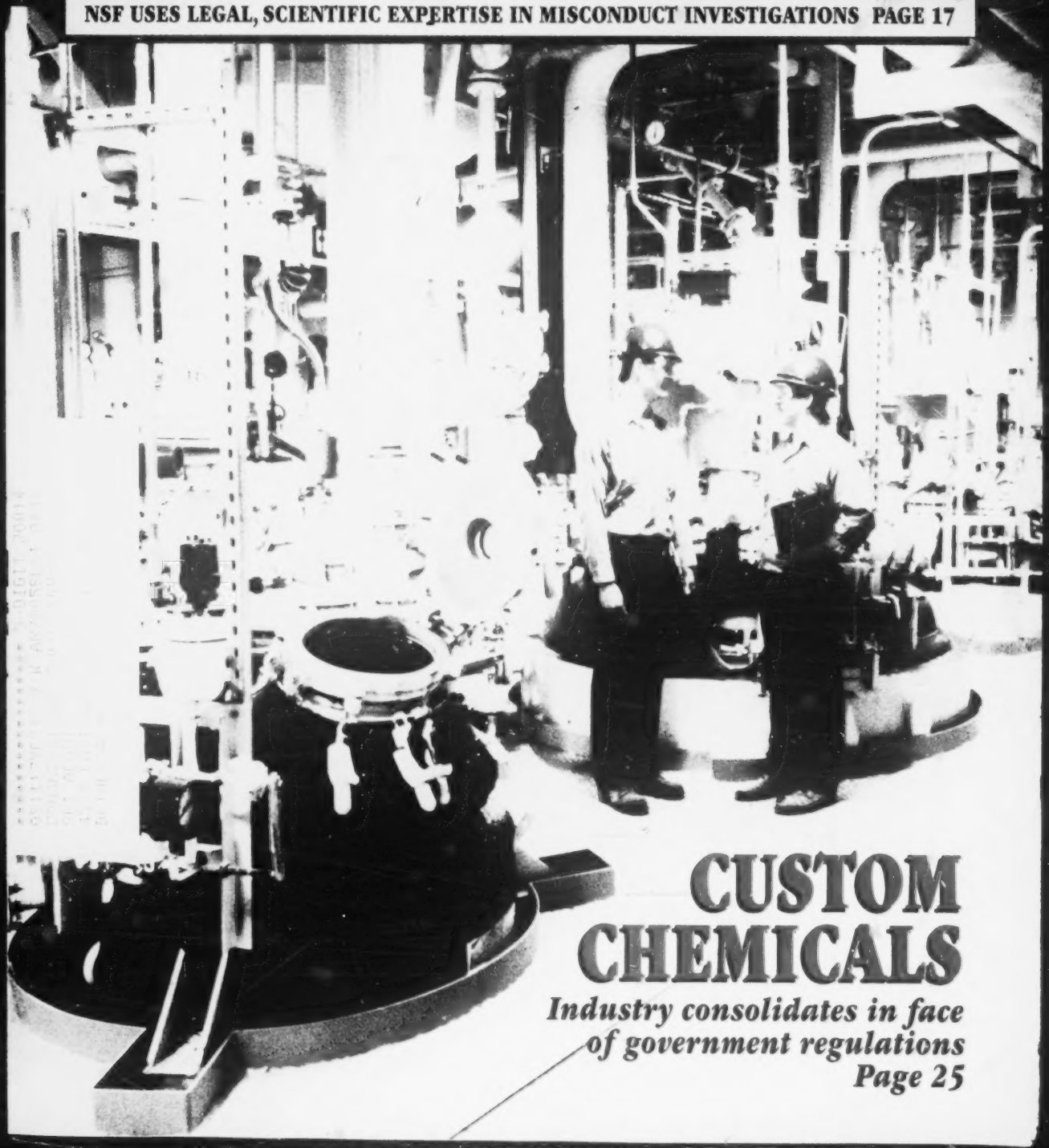
CHEMICAL & ENGINEERING NEWS

C&EN

FEBRUARY 3, 1992

NSF USES LEGAL, SCIENTIFIC EXPERTISE IN MISCONDUCT INVESTIGATIONS PAGE 17



CUSTOM CHEMICALS

Industry consolidates in face of government regulations

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CHEMICAL & ENGINEERING NEWS

C&EN

FEBRUARY 3, 1992

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- President Bush emphasizes importance of R&D in State of the Union address and sends a budget to Congress that calls for a 3% increase in overall R&D funding in 1993. Page 4
- Despite poor chemical company earnings and sales in the fourth quarter of 1991, analysts are optimistic and are recommending chemical stocks. Page 5
- Congress' scrutiny of indirect costs charges continues with investigations of Superfund and Department of Energy contractors as well as universities. Page 6
- Monsanto Chemical starts program that gives employees $1000 toward purchase or lease of vehicles built in North America. Page 6

COVER: Aldrich Chemical's custom chemical facility near Sheboygan, Wis.

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BUSINESS

Chemical firms see ties with universities as important part of their research and development programs, although relationships occasionally can be strained. Page 9

Canadian companies are optimistic about their prospects in 1992, following a bad year for the chemical industry when pretax profits virtually disappeared. Page 13

Plastics packaging firm, Ametek, has profited from new proprietary blowing agents and reusable and recyclable packaging systems developed in response to concern for environment. Page 14

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At NSF, allegations of scientific misconduct are handled by small team of scientists and lawyers in agency operation that, unlike NIH's, has so far escaped controversy. Page 17

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Taiwan readies for high-tech era, with science and technology among government's top priorities and R&D budget over the past few years up an average 24% annually. Page 21

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In "The Green Flame: Surviving Government Secrecy," Andrew Dequasie gives little detailed technical information about nearly 40-year-old defense-related project, but provides historical account of his personal experience. Page 52

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Forty-six student affiliate chapters have been recognized for their programs and activities for the 1990–91 academic year by ACS's Society Committee on Chemical Education. Page 53

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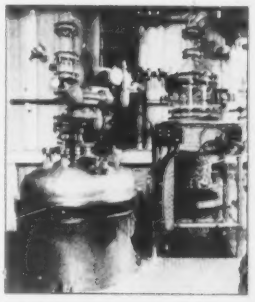

Custom chemical producers move to meet changes occurring in fine chemicals industry in their effort to stay competitive into next century. Page 25

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LETTERS

CHEMICAL SAFETY

Perfluorocarbon compounds and polymers

There was a serious error in my letter on the potential hazard posed by perfluorocarbon compounds and polymers in combination with strong oxidizers (C&EN, Dec. 16, 1991, page 2). Although these compounds can burn with the release of significant energy in some circumstances, this error greatly exaggerated their theoretical hazard in high-pressure oxygen.

The corrected ideal-gas results for varying weights of two perfluorocarbons in a 110-cc bomb containing oxygen at 2000 psi are as follows:

	Grams							
	0.20	0.25	0.40	0.60	0.80	1.0	5.0	10.0
C_7F_8								
T (K)	463	502	613	750	878	998	2591	3386
P (MPa)[a]	21.48	23.30	28.51	35.00	41.05	46.78	130.39	197.75
P (psi)	3115	3379	4135	5076	5954	6785	18,911	28,681
Polytetrafluoroethylene								
T (K)	374	392	446	514	578	639	1482	2090
P (MPa)[a]	17.34	18.20	20.74	23.98	27.07	30.0	73.93	112.43
P (psi)	2515	2640	3008	3478	3926	4351	10,723	16,307

a Megapascal.

The results for TNT in my previous letter were correct, but they were for 19.965 g (based on 0.25 g of perfluorocarbon + 19.75 g of oxygen), not 0.43 g. The corrected pressures are much lower than the TNT results, so the comparison has little significance.

I thank Kirby Scherer and R. Bert Diemer (Du Pont Polymers) for a valuable discussion on these calculations.

Eli Freedman
Baltimore, Md.

Bottled water

A Newscripts item (C&EN, Dec. 16, 1991, page 40) referring to a *CHEMTECH* article on bottled water, noted that of the 37 waters analyzed, 24 were out of line with one or more requirements of the U.S. drinking water standards, and quoted, "It is unlikely that a survey of community water supplies would find as high a degree of noncompliance. Maybe we'd all be better off drinking tap water!"

While ACS decries the public's lack of understanding and trust of science, ACS publications should not be carrying *Reader's Digest*-grade articles. These authors either misrepresent, or do not understand, drinking water standards.

The impurities cited as exceeding the U.S. drinking water standards include: pH, chlorine, fluorine, manganese, sulfate, and barium. All of these (except barium) are secondary drinking water standards, which EPA states are "not designed to protect the public health. Instead they are intended to protect 'public welfare' by providing guidelines regarding the taste, odor, color, and other aesthetic aspects of drinking water which do not present a health risk."

Although the European Economic Community has chosen to set low guideline levels for calcium (100 mg per L), magnesium (30 mg per L), potassium (10 mg per L), sodium (20 mg per L), and chlorine (25 mg per L), these are essential minerals for which humans have substantial daily requirements. For comparison, whole milk contains (per liter) 1190 mg calcium, 130 mg magnesium, 1500 mg potassium, and 490 mg sodium. Why should a water with comparable mineral content be considered dangerous?

So let's be reasonable about water. There are plenty of other items that are truly harmful, and most people don't like the taste of distilled water anyway!

Eugene J. Kuhajek
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Morton International Inc.
Woodstock, Ill.

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Corporate Execs Weigh Evolving University/Industry R&D Alliances

■ ***Although relationships have been strained at times, industry looks positively on improved ties to academia***

Ann M. Thayer,
C&EN Northeast News Bureau

The "cultural gap" between industrial and academic research continues to take on interesting new dimensions as relationships between companies and universities evolve. In the past, debate has centered largely on the inherent shortcomings of such alliances because of the different paces, outlooks, and goals in industrial and academic research. At the root of this is a mistrust and fear that academia will be subverted by commercial interests, which in turn misunderstand and misuse university research.

Changing attitudes, as expressed by chemical industry executives, suggest that alliances are moving in new directions. Among these is an apparent awareness of industry's and academia's complementary roles in R&D. Whereas companies say they have become more flexible in negotiating agreements, ironically universities are said to be moving in the opposite direction. Counter to this, universities are at the same time being pulled toward working with industry as a result of declining federal support.

In 1990, $1.14 billion of the $16.3 billion in funding for academic R&D came from industry, according to the National Science Foundation. Although this is well below the $9.6 billion from the federal government, industry's contribution has risen from about 4% to 7% over the past decade. The federal government's contribution has fallen from 67% to 59%, while other sources of funding, except institutional sources, have remained flat.

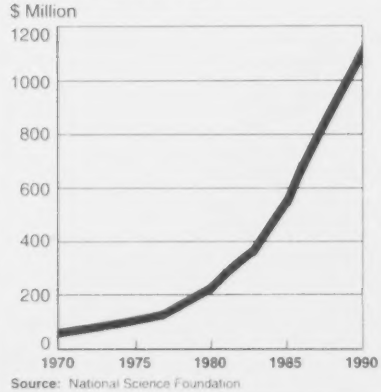
Despite industry's increasing financial commitment to academic R&D, questions continue to arise over intellectual property rights, conflicts or lack of interest on the part of university researchers involved with commercially related research, the demand for rapid returns on investments by industry, and the function of universities to publicly disseminate scientific results versus the need by companies to retain proprietary information. The remarkably similar views of executives from six major chemical companies—Dow Chemical, Du Pont, W. R. Grace, Hoechst Celanese, Monsanto, and Union Carbide—suggest that these issues are being addressed in the way collaborations are established.

Although collaborations with universities may differ in detail, the philosophy and goals behind them are very similar. "To ignore academia is to ignore a tremendous pool of talent and creative ideas," says Frank Knoll, project manager of cooperative research, Dow Chemical corporate R&D. "There's nothing that says a company can't do that, but I think . . . it would be a poor decision." Faced with competitive pressures based on the ability to make technological advances, chemical companies see alliances as an important element of their R&D programs. There is a need for fundamental research in support of core technologies and product development, and for accessing emerging technologies as a means to stay competitive. For small companies with limited resources, such as biotechnology companies, alliances can provide a primary source of basic R&D and licensable discoveries.

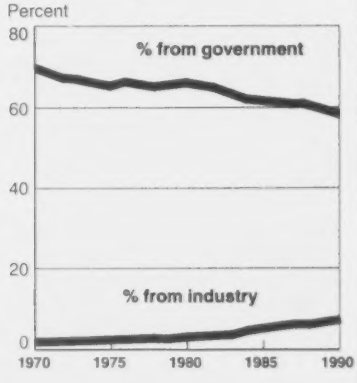
"Grace has no hesitancy to start at a very fundamental level in new research fields that the company can identify as having long-term impact on our product lines," says F. Peter Boer, a Grace executive vice president and chief technical officer. "The company uses university relationships to further its total strategy when it comes to innovation, long-term research, and even some medium-term problem solving." In return, industry not only helps support basic research but, when the occasion arises, also provides the development tools to commercialize university discoveries.

"For the most part, I feel very strongly that truly basic research, and by that

Industry support of academic R&D is growing . . .



. . . as is its share relative to government



Source: National Science Foundation

I [mean] research which has as its express purpose the creation of new knowledge in a specific field, is best done in academe," says Leonard N. Baker, vice president, corporate technology at Union Carbide. The company participates in about 30 university-based consortia and has more focused research agreements with about 20 other universities. Many firms also have relationships with foreign universities as a means to tap into research developments or to have a company R&D presence overseas. "[Union Carbide] feels strongly that it has to stay on top of cutting-edge technologies in areas that are related to its core competencies," Baker adds. "These contacts are a way of focusing and leveraging the company's R&D sources in areas of potential significance to the corporation."

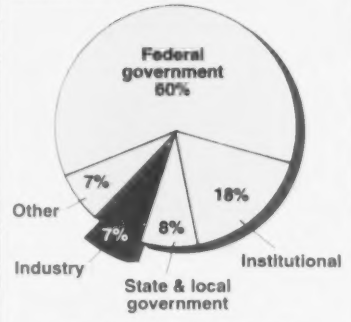
Monsanto's 10-year alliance with Washington University Medical School, one of the oldest and largest collaborations between a U.S. company and university, is an example. Deciding in 1981 to enter pharmaceuticals and realizing that it would take decades to build up an in-house effort, Monsanto looked at a university alliance as a means to access basic R&D discoveries, explains Philip Needleman, who came from the university and is now Monsanto's vice president for R&D and chief scientist.

The success of the program in its first few years accelerated Monsanto's acquisition of its Searle pharmaceutical subsidiary in 1985, Needleman believes, giving the company a development arm with which to move discoveries forward. "As to the company strategy," he says, "the university arm is an ideal complement to its own internal research program." With a second program renewal in 1990, total funding commitments reached nearly $100 million. Currently about 50 projects involving 120 university scientists are supported.

Despite a few product leads, the Washington University program needs "refinement," says Needleman, and to move away from its broad scientific goals. "We did a great job in taking care of what the university needed, and a good job of what Monsanto needed in terms of a menu [for development]," he says. "But this program only will go on if we both can succeed.

"We have had a great first decade, but [Monsanto] needs to focus more on a limited number of disease areas so that we can advance more expeditiously through discovery and toward effective therapeutic agents." Although not wanting to leave the present arrangement with Washington University, he adds that he would not choose to enter a large university agreement again. "I don't see the advantage of taking large grants into a broad program as opposed to surgically picking the specific areas the company would like to advance and develop."

Industry funds 7% of academic R&D



Fiscal 1990 academic R&D spending = $16.3 billion

Source: National Science Foundation

What is difficult to gauge is whether these alliances represent either a decreasing internal investment or an increasing overall commitment to basic research on the part of chemical companies, and the implications of this. In most cases, the alliances are separate from more straightforward licensing functions. "In the past, it's been traditional for Du Pont to bring [new] technologies in-house either by licensing patents or hiring the right researchers," says James Nottke, director of technology acquisition for Du Pont. "These days the company wants to look more broadly to see if it makes more sense to support a professor's research."

Du Pont created Nottke's position this year with the strategic goal of exploring technologies to pursue and to expand the firm's contacts with universities. Du Pont's ongoing collaborations generally have been set up on an ad hoc basis, and Nottke sees his new centralized role as initially identifying and "brokering" relationships, but then stepping back. "I will be looking for those pieces that will take us into some pioneering areas, building on some of our core competencies," he says. "Very seldom does a company really strike out in a field that it is totally unfamiliar with. It usually fails if it tries." Similarly, in the late 1970s, Dow created its centralized office in corporate R&D to help coordinate and fund interactions among Dow researchers and academic scientists and to screen proposals submitted to the company.

For companies, collaborations can be cost-effective routes to explore new technologies without committing resources or hiring staff at early, and more risky, stages of development. During recession, research objectives still can be accomplished when companies are faced with hiring freezes, thereby freeing up limited internal resources that can be applied elsewhere. To estimate the value to companies, one need only consider the relative proportion spent by companies and universities on basic versus applied research projects. "There is no company in the world that is spending what Washington University is in fundamental discovery," says Needleman. "So in academic life there is more 'bang for the buck' at the discovery level than there is in industry. Yet, what academic life doesn't do is advance that to the [ultimate product]."

A pitfall to avoid, companies have learned, is using universities for product development, something for which they generally are not equipped or necessarily interested in doing. Trying otherwise has been a criticism of industry programs with universities and generally only results in frustration on the part of the company and resentment on the part of the university. "If we find something that looks like it would fit well with our business strategy and product line, there are occasionally the temptations to use the people at the university to do the next stage of development because they are already [involved in the project]," says Nottke. "But they will always do it a little slower and without a number of the manufacturing concerns that we in industry have."

In light of this, it is no longer surprising that most collaborations by chemical companies are aimed at accessing universities' expertise in basic research. "Universities, in doing fundamental research, have two products," says Baker. "One is scientific knowledge itself

and the other is the mechanism by which that knowledge is generated, and that mechanism is students." And, it is these types of relationships that companies now believe are the most successful.

For collaborations to be deemed successful, most managers say there need not be tangible results and many accept that success rates will be low. In fact, examples of actual products that have come out of chemical company and university collaborations appear limited, although some companies can cite numerous patents. "If [commercializing products] were used as a criterion, then Dow might ask the question: Is cooperative research really successful because it doesn't have a specific product to show for all this?" says Knoll. "But the company thinks that the real value is in the collaborative and creative interactions that have occurred over the years and continue to occur.

"Patents and intellectual property are an important part of the deliverables in a program," he adds, "but you get very good results very often where no patents develop." Instead, information that contributes to a basic scientific understanding in support of a company's product or technology development generally is considered the most positive result. And measuring the success of a program depends largely on the expectation level set in the very beginning.

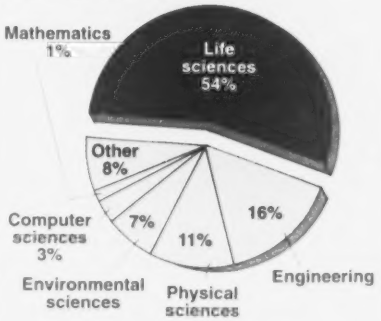
"Some companies may go in with marching orders," adds Knoll, "Dow doesn't. If you understand how universities and students and the education process work, you can't really demand that kind of thing. I think there are companies that have the mentality that [universities] are like research institutes and ask for specific deliverables, but in fact they are not contract research institutions. When you develop a university interaction, you want to tap into the creative abilities of a professor and a student and that's a variable thing."

If companies and universities can bridge the differences in outlook and pace of industrial and academic research, believes Boer, "the other problems are easy." Another factor in success is a strong common objective. "Like curing diabetes, that's a powerful objective," he explains. "Powerful to W. R. Grace and its stockholders because it has financial and social value, and powerful for a university because it has social and academic value." Development of an artificial pancreas, now in advanced preclinical trials, is one of Grace's largest programs based on university collaborations.

Collaborative projects tend to be negotiated on a case-by-case basis and therefore run a gamut of styles. An important caveat, comments one executive, is to not cross the line between research contracts that have strings attached and philanthropic grants, otherwise both their management and messages get confused. In general, projects last from one to a few years and are reviewed at various stages for renewal. "Dow usually tries to avoid multiyear commitments," says Knoll, "because it is very common to discover things that we didn't expect, so [renewing] is a very convenient way to refocus the project and it also allows us to check on progress." Based on experiences from an earlier, failed program with Harvard, Monsanto uses an external review panel in its program with Washington University.

Funding typically ranges from about $25,000 to $50,000 per project, but can go as high as $100,000 or $250,000, depending on the number of faculty members and students involved. Total investments by a company are difficult to estimate because most have a wide variety of ties with a number of universities through faculty consultants, unrestricted grants, fellowships, collaborations, and memberships in consortia.

Universities spend most on life sciences



Fiscal 1990 academic R&D spending = $16.3 billion

Source: National Science Foundation

On average, total annual funding for cooperative R&D is about a few million dollars for each company, although Du Pont and Monsanto spend a few times that amount. Although a relatively small proportion of their R&D budgets, chemical companies consider their investments as sizable and take them very seriously.

Further complicating estimates is that most funding comes from individual R&D divisions or business areas within a company, as do the initiatives to set up collaborations. An exception, but only in terms of funding, is Dow's cooperative research office, which carries the majority of costs in the first year and then splits costs with sponsoring Dow labs in later years. Having separate R&D or business areas responsible for funding operates as a system of "checks and balances" on how resources are invested, along with determining the importance of, and commitment to, specific collaborations.

A few chemical companies indicate that they may try to avoid overlapping on projects with federal funding because government restrictions can limit access to certain technologies. However, others believe that this is not a serious limitation or are willing to accept whatever restrictions may arise. "In recent years, the government has been insisting that in some federally funded contracts there also be industrial partners so that technology transfer from the university to private industry is facilitated," adds Baker.

Most companies set up some sort of research agreement or contract that deals with the disposition of intellectual property rights. Patents, if they result, frequently belong to the scientist or university under its rules, although industrial patent offices often assist in the preparation and filing of patents. Companies commonly ask for right of first refusal for exclusive licenses to university patents, although other provisions may be made with determining factors related to the area of research and level of investment by the company.

Restricting publication of results has been harshly criticized and companies find moves in this direction meet with resistance by universities, which guard this right carefully. Because more collaborations are aimed at fundamental, rather than proprietary, research, the consensus on the

part of chemical company managers is that all work is publishable. It still is common for companies to ask for a period in which to review any results before they are made public, while trying to ensure reasonably prompt publication and open discussion of scientific results. "If a company is greatly concerned about proprietary information being involved," says Boer, "it shouldn't enter into a university relationship."

Despite what industry sees as an increased flexibility on its part in structuring alliances, there is a sense of more rigidity on the part of universities. Evidence of this is a move on the part of universities to retain technology, or at least the control of rights to it, say company managers. A less extreme view is taken by Carbide's Baker, who suggests only that universities have become more aware of the value of patents and that industry should be aware of this and willing to work out a few issues.

"There was a time when university patent offices were operating under some significant misapprehensions and were functioning more to protect the university from an unknown evil than to foster the commercialization of their technology," says Boer, leading to "onerous" terms. These misapprehensions were fueled by a few cases in which patents, such as the Cohen and Boyer fundamental patent on the process for inserting genetic material into bacterial plasmids, have generated large revenues for universities or researchers.

"Every university felt that it must have such things just around the corner," says Boer, "when in fact there are very few Cohen and Boyer [patents] out there. It is very important for a university to understand that the licensing terms should also be on a basis that is attractive for the industrial partner to continue the project and to take the risks toward commercialization."

However, universities are faced with increased pressures to find funding and may look to generate revenues from their patents. But companies stress that while universities may want to do this, it is time-consuming to build up patent libraries, to license technologies, or to try to develop products when they lack any real experience. "Universities don't worry about markets and product economics as they are not in the business of doing that," says Knoll. "Whereas Dow, as with any company, lives and dies by its ability to evaluate the worth of any technology in the marketplace."

"Universities often overestimate the dollar value of a discovery," says Faruq Marikar, manager for external technology at Hoechst Celanese, "and misunderstand the process of innovation in industry, which is usually incremental rather than one big leap." Contributing to this problem, he adds, is legislation that allows universities to have exclusive rights to government-funded research inventions. "Universities are trying to use the same policy on work that industry funds." In response, he explains that companies look carefully at how much, by way of licensing, university patents really are worth and, believing it unlikely that many will generate income, have become more lenient about patent rights.

Universities viewing companies only as a source of money also can be counterproductive, say chemical industry executives, but this can sometimes be related to how strong the connections are between a company and a university. "Dow tries to reach an understanding with the university that this truly is a collaborative effort with close communication between the Dow scientist and the academic scientist," says Knoll, "both contributing ideas, working closely together, and getting excited about the progress."

Another factor can be the level of management at which projects are handled. The most positive relationships and successful collaborations come about from a "bottom-up" rather than a "top-down" approach, say chemical company managers, based on the idea that people, rather than institutions, are working together. Many collaborations are initiated by individual company scientists who have a strong interest in working with a university researcher. For this reason, most also are set up on an ad hoc basis.

"I feel very strongly that 'bottom-up' is the way to go," says Boer. "Basically, you won't do very well if you don't have an internal scientist who is enthusiastic about the area of research, in essence taking responsibility for the program, and generally as knowledgeable about it as his university counterpart." Although their areas of expertise or knowledge may be somewhat differently oriented, he explains, together they make a motivated team. This feeling of teamwork also tends to create a sense of seriousness about the program and that "a company is not just talking about easy money for a few years, but that real results and a deep relationship are expected," he adds.

Proximity also can play an important role in initiating and sustaining relationships between chemical companies and universities. Close relationships with universities allow companies not only to access research developed in collaborative projects but also help to expand connections to the scientific community in general. Chemical companies ask their researchers to stay on top of developments and to be aware of leading academic scientists in areas of interest to the company both as a means to manage and improve ongoing collaborations, and to scout for new alliances.

On the chemical company side, it also is important that there are strong in-house R&D efforts to draw on, employ, or adapt work done at universities. "There is a limitation on how much technology and basic science a company can go out and acquire from the university system," says Marikar. "Ultimately it is limited not by the dollar amount, but [by] the technology expertise a company has in the way of people who can go and [work with] the university system."

Although not the main reason behind most collaborations, say company executives, alliances do provide a means to evaluate students as candidates for hiring, and students can make contact with potential employers. Hiring students who have worked in research areas of interest to a company is one way to transfer technology development in-house. And students who stay in academia also are possible future collaborators.

But overwhelmingly, chemical executives say they are not looking for individuals trained to do applied research. "We need more scientists and engineers in the U.S. to maintain our competitive capabilities," says Carbide's Baker. "And any enlightened high-tech company would much rather have highly trained, sophisticated, and versatile individuals trained in the true academic sense, but interested in applying that knowledge to commercial problems." □

Belanger contends that the next major cycle of global chemical investment is being planned now. It's critical, he argues, that governments restore competitive tax policies for the chemical industry as soon as possible. If they don't, "there's a very real risk that Canada will be left out of the next wave of expansion," he warns.

But tax problems aren't the only thing bothering Canadian chemical companies. Canada's exchange rate policy, which has kept the Canadian dollar strong, has hurt exports and boosted imports. Pending legislation in Ontario, including labor legislation, also worries the Canadian chemical industry.

Despite the pall overshadowing the CCPA survey, Canadian chemical companies are "cautiously optimistic" that the worst is behind them. Sales are expected to increase 5 to 6% in both value and volume. And although sales to domestic customers will inch upward only 1%, exports probably will increase 10%, including an encouraging 16% increase in shipments to the U.S.

Still, these forecasts could be overly optimistic if the hoped-for improvement in economic conditions doesn't materialize. In addition to the questionable North American economy, Europe's economy also is softening. So, too, is Japan's.

Many chemicals still are in oversupply. Among them are ethylene, polyethylene, and sodium chlorate, products that are particularly important to the Canadian chemical industry. It will take time to work off this surplus.

In time, the restructuring and adjustments that Canadian chemical companies have been making will put them in a good position to capture new business in the U.S.—that is, when business conditions there improve. One company says that, increasingly, U.S. customers are beginning to accept Canada as a "valid North American source."

According to the CCPA survey, the best hope for the long-term growth of the Canadian chemical industry lies in integrating production and markets on a "North American" basis under the Canada-U.S. Free Trade Agreement. Unfortunately, the industry believes that the benefits that should come from such tactics are threatened by the Canadian government's own economic policies.

Lael Anderson

Environmental push pays off for packaging firm

Environmental groups often attack packaging materials because the process to make them may release potentially toxic chemicals, and then, used once, packaging materials take up valuable landfill space. Ametek, a diversified manufacturer based in Paoli, Pa., believes it can answer environmental activists' objections and make good profits at the same time.

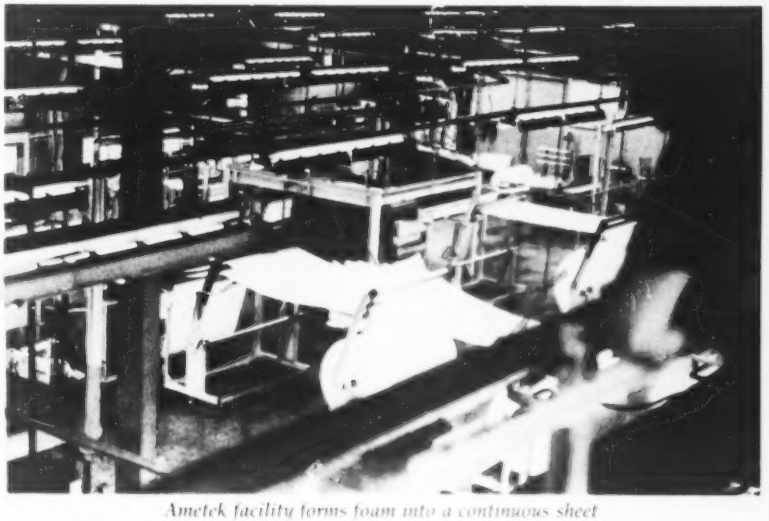
The company's Microfoam division, headquartered in Chadds Ford, Pa., had been using chlorofluorocarbons (CFCs) as blowing agents to produce polypropylene packing sheet foam for shippers of sensitive electronic equipment. Now it has replaced these CFCs with proprietary blowing agents, and has perfected a process to capture and reuse these blowing agents. Microfoam also has come up with reusable and recyclable packaging systems for furniture shippers.

Herman C. Koch, general manager of Microfoam, admits the company was under government pressure to replace CFCs in the production of polypropylene foam packaging materials. CFCs have been implicated in the destruction of Earth's protective ozone layer. Development of a replacement for CFCs began four years ago at Ametek, says Koch. As far as Ametek is concerned, the replacement blowing agents "have been a positive environmental trend."

Ametek does not, however, use a hydrocarbon blowing agent, which competing polyethylene foam sheet producers use. Hydrocarbon blowing agents are volatile and unsafe if improperly handled, Koch points out. In addition, unrecovered hydrocarbons can contribute to the formation of atmospheric smog. The environment and safety were major considerations in the three years of work Ametek invested in its proprietary blowing agent system, he says. The resulting system poses little threat to workers and is environmentally sound, he claims.

The new system allows Ametek to recover up to 99% of the blowing agents used to produce its packaging foam sheets, Koch says. Recovery and reuse not only pays for construction of the recovery system at the company's plants (a $5 million expenditure), but also justifies the higher initial cost of the blend itself, he notes. Ametek actually saves money because of the recovery and reuse of the new blowing agents.

Government and environmental groups not only have forced packaging manufacturers to change their practices, but also have had an effect on packaging users. More industrial shippers are reducing the volume of packaging materials they use, and getting rid of multilayer packaging made of dissimilar polymers. And recently enacted and impending government regulations have prompted shippers to eliminate



Ametek facility forms foam into a continuous sheet

Koch: recover up to 99% of blowing agents

unnecessary packaging, employ reusable containers, and recycle.

A good example is furniture maker Ethan Allen, Danbury, Conn. The company separates and sells used packaging to recyclers, and takes back packaging from its dealers for recycling, points out Thomas Lowery, director of packaging and engineering. It does not limit recycling to the type of polypropylene foam that Ametek supplies, but also recycles other packaging materials such as polyethylene, polystyrene, corrugated cardboard, and even wood skids—all of which have their use in packaging goods so they may be shipped safely and without blemish.

Retailer Sears Roebuck & Co. announced in November that it was working with suppliers to reduce packaging volume 25% by 1994, thereby eliminating 1.5 million tons of packaging materials by the end of 1994. Pressured in part by customers, Sears hopes not only to help reduce the nationwide solid-waste disposal problem, but also to save $5 million. Another of its goals: By the end of 1995 plastic containers used to package its products will contain 20% recycled material.

As the government, major manufacturers, and retailers put pressure on the packaging industry to reduce waste and recycle packaging materials, it is in the best interest of packaging manufacturers to respond. After all, they will want to preserve the U.S. protective plastic packaging market, which market analysts Kline & Co., Fairfield, N.J., estimates has sales of $1 billion annually and projects to grow at about 5% annually over the next few years.

Koch wants to see his company grow faster than the industry, and the key is weight reduction and reuse of shipping containers. In fact, Koch hopes sales of Ametek's polypropylene foam will continue to increase in the next five years at the current 10% average annual rate. Though declining to give precise data for competitive reasons, Koch says foam sales are between $30 million and $50 million. That would give Ametek between one third to one half of what Kline & Co. estimates is a roughly $100 million foam sheet protective packaging market. Ametek does not break out division profits either. Net income for the company's 15 divisions was $37.3 million on sales of $661 million in 1990.

Ametek is the only U.S. and worldwide producer of low-density polypropylene foam sheet, according to Koch. The foam is produced via a proprietary flash extrusion process that Du Pont developed but sold to Ametek in 1983 to raise cash after its purchase of Conoco, he says. Production is rapid: At speeds approaching those of paper production, the foam is formed into a continuous sheet at Du Pont's original plant in Wurtland, Ky., and a newer plant in Fresno, Calif. A third plant is under construction in northwest Maryland, he adds.

Packaging sheet foam competitors include low-density polyethylene foam sheet and plastic bubble wrap producers. AVI Corp., Glens Falls, N.Y., and Sealed Air Corp., Saddle Brook, N.J., manufacture both types of plastic packaging. Other packaging competitors include manufacturers of macerated paper pads, cellulose wadding, and a type of corrugated cardboard with one smooth side.

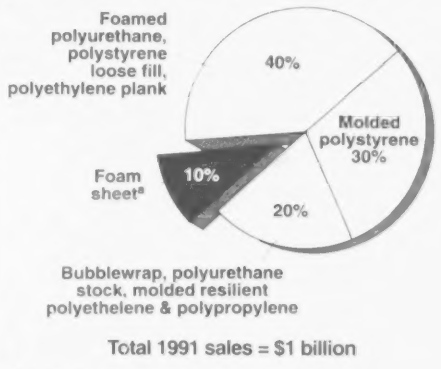
An Arco Chemical joint venture with Japan Styrene Paper and Mitsubishi Gas Chemical produces expanded polypropylene foam beads in the U.S. for sale to packaging manufacturers. However, Amoco and its partners do not sell a sheet foam. A manufacturer molds the beads into appropriate shipping packages. Ametek's closest plastic packaging competition, polyethylene foam, has a density of 1.2 lb per cu ft compared with 0.6 lb per cu ft for polypropylene foam. Koch says the low-density Ametek foam reduces the amount of polymer necessary to manufacture a cubic foot of foam, which ultimately means less waste should the material be discarded. If the polypropylene foam must be discarded, Koch says it would make more sense to incinerate it because it is "a good source for energy."

But a new shipping container, which the company refers to as a "couch pouch," will encourage reuse as well as recycling, says Koch. The couch pouch is a composite of polypropylene sheet foam and nonwoven polypropylene fabric that Ametek produces in eight sizes to enclose furniture. He says they may be reused five times or more, only cost 15% more than one-use paper bags, and weigh 75% less than paper.

Other polypropylene foam uses the company is working on for its sheet foams include packaging for fruits such as apples and pears. Among small but developing markets are use as concrete curing blankets in place of glass fiber, insulation for greenhouse knee walls, and underlayment for flat asphalt roofing systems. It also may find use in oil-spill containment curtains because of the foam's buoyancy, flexibility, light weight, and ability to absorb light oils.

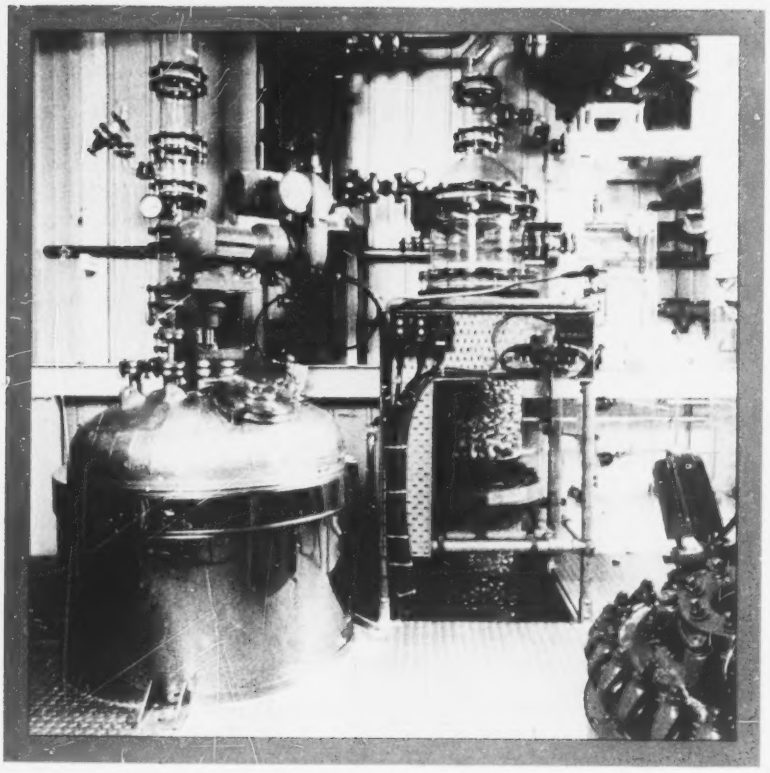
Marc Reisch

Foam sheet is now only 10% of protective plastics packaging market



Total 1991 sales = $1 billion

a Polyethylene and polypropylene. **Source:** Kline & Co.



Stainless steel reactor at Newport Pharmaceuticals Ireland can handle reactions carried out at –100 °C

Custom Chemical Producers Set to Meet Industry Changes

Stephen C. Stinson,
C&EN Northeast News Bureau

Widespread changes rippling through the fine chemicals industry have also had an impact on the business of custom chemical production within that industry.

Among these changes are a wave of consolidations through mergers and acquisitions; a trend to more complex molecules tailored to customer needs; greater willingness even by large firms to seek outside sources of chemicals; stricter requirements for chemical product quality; and tightening regulations on pollution, waste disposal, and safe production and transportation.

As a result, the fine chemicals industry and its custom production segment must adopt several production strategies to be successful in the next century, according to Enrico Polastro, fine and specialty chemicals director at Arthur D. Little International in Brussels. First, companies should establish a balance between the efficiency of single-purpose facilities and the flexibility of multipurpose facilities. Companies can use single-purpose units to produce a steady stream of standard catalog compounds to balance out their custom production on the multipurpose equipment.

Second, Polastro says, companies must participate in the consolidation of the industry to attain the minimum size needed for survival. A minimum size is needed to justify the investment in production safety, pollution abatement, and waste disposal. He suggests this size is $50 million per year in sales.

And third, companies must avoid obsolescence of technologies and equipment in an age of rapid evolution of types of chemicals demanded. They must create a balanced portfolio of production technologies, including key technologies not widely available that turn out high-value-added products.

Sales of the world fine chemicals industry are about $45 billion per year, estimates Zack I. Levine, vice president and general manager of the Hoechst Celanese fine chemicals division. Of this, 50% is drugs, 20% is pesticides, 5% is aroma chemicals, 5% is food additives, and 20% is "other," which includes high-performance polymers, monomers, and plastics additives, reprographic chemicals and photoresists, and colorants. The U.S. market is $15 billion, he says, and is growing at about twice the gross national product.

How much of this is custom production is hard to estimate. Much custom work is one firm making a unique compound for one client with the compound's value shrouded under secrecy agreements. And some large companies that do custom work on the side only do so to use spare kettle space. Analysts at Kline & Co., Fairfield, N.J., have put U.S. custom production at $1.7 billion per year.

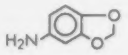
Levine cites a shift toward greater molecular complexity as an opportunity for fine chemicals makers. Especially in the drug industry, molecules are more highly designed to perform a predetermined function. As Levine puts it, "All of the simple molecules have been discovered."

Because of greater targeted effectiveness, smaller volumes of fine chemicals production will be needed. The opportunity here is that supplier firms can increase versatility and responsiveness as their clients grow reluctant to produce small volumes themselves. But as competition grows among end users of fine chemicals to design for the same disease or functional property, the life cycle of any one fine chemical will be shortened. "This could present a real

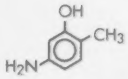
Organic Intermediates

for pharmaceuticals, agrochemicals, dyestuffs, flavors, fragrances, photochemicals, etc.

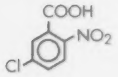
3,4-Methylene-dioxyaniline and N-Ethyl derivative



5-Amino-o-cresol



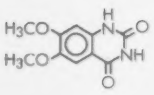
5-Chloro-2-nitro-benzoic acid



Dodecylaniline (isomer mixture)

2-Ethylphenol

6,7-Dimethoxy-quinazoline-2,4-dione



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- Nitration
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US-Agents:
Henley Chemicals, Inc.
50, Chestnut Ridge Road, Montvale
NJ 07645, Phone (201) 307-0422
Fax (201) 307-0424

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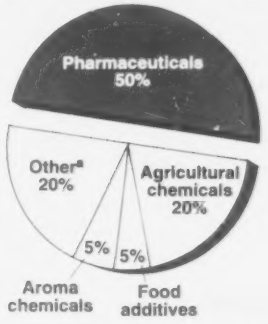
Pharmaceuticals account for half of fine chemicals sales



1991 worldwide fine chemicals sales = $45 billion

a Includes plastics, monomers, and additives; reprographic chemicals and photoresists; and colorants
Source: Hoechst Celanese

opportunity for smaller, more rapidly moving organizations and a major obstacle for large, more highly structured organizations," Levine says.

In another area, that of consolidation and growth by acquisition, two of the most active companies in the U.S. have been Cambrex Corp., Bayonne, N.J., and MTM of Cleveland, England.

Cambrex came into being when NL Industries spun off its Baker Castor Oil Co. as an independent in 1981. Since then, the company has acquired Cosan Chemical Corp. (1985), Nepera (1986), Heico Chemical and Humphrey Chemical Co. (both 1989), and Salisbury Chemicals (1991). Cambrex is currently negotiating with Hexcel Corp. to acquire that company's chemical products division. Combined sales from all sources were almost $140 million in 1990.

Though all these components are far flung, the custom synthesis business for all of them is handled by Stuart Needleman at the Cambrex plant in Carlstadt, N.J. He prospects for new custom business, and subsidiaries refer any inquiries to him. Needleman sits on committees of each subsidiary to evaluate new proposals for profitability and environmental concerns.

In keeping with Polastro's call for key technologies not widely available, Needleman can offer nitration, metal reductions in liquid ammonia, high-pressure hydrogenation, and chemistry involving mercury and arsenic. As Needleman quips, "We're looking for

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situations in which we have an unfair advantage over the competition."

In particular, nitration is a dangerous process itself, and the resulting nitro compound also may be explosive. So rather than take delivery of a nitro intermediate, customers may prefer to let Cambrex proceed with a reduction process. The upshot may be that Cambrex gets to do all of a multistep synthesis because of the nitration and reduction in the middle.

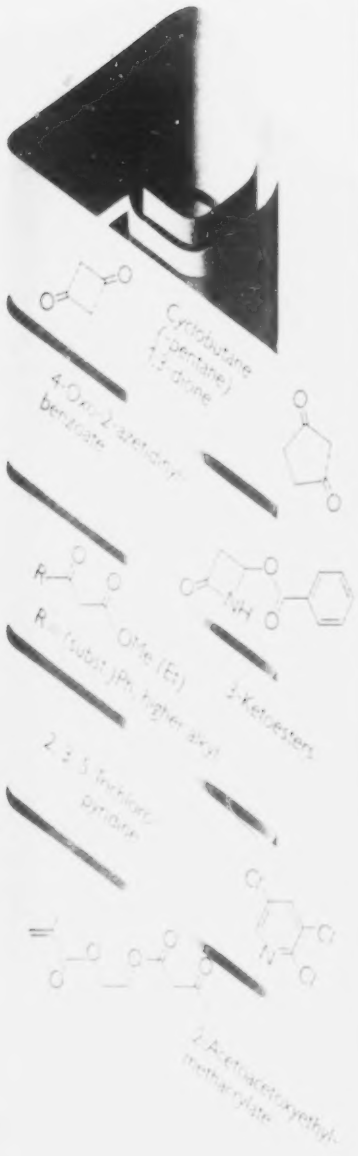
Chemistries of the Cambrex subsidiaries are complementary too, so integration among them is possible. Says Needleman, "We have one ongoing project where Humphrey makes the starting material, Heico does the next step, and Salisbury does the finishing step."

Acquisitions also have been a spur to growth during MTM's move into the U.S. The company began with a sales office in Houston in 1983. In 1988 MTM bought Fairfield Chemical Co. and Draybor. And in 1990, MTM Chemical got the Orsynex subsidiary of Essex Chemical Corp. after Dow Chemical USA acquired Essex in 1988. Farchan Laboratories, Monomer Polymer Corp., and Hardwicke Chemical Co. also were bought in 1990.

Though the company has many subsidiaries organized under the two umbrellas MTM Chemicals and MTM Research Chemicals, executive vice president John Luvisi is the contact for custom production. Luvisi, who is with MTM in Charlotte, N.C., can arrange business within MTM according to the quantities needed, the chemistries required, and whether the customer needs a Food & Drug Administration-approved plant.

In other activity, Outokumpu Metals & Resources of Helsinki, Finland, formed a new company, OM Group, Cleveland, Ohio, in 1991, which acquired Mooney Chemicals of Cleveland; Outokumpu Chemicals of Kokkola, Finland; and Vasset of Ezanville, France. OM Group makes a standard line of metal carboxylates and also produces such compounds to order.

Burnham Tinker, vice president for research and development, says the OM Group has technology to make metal carboxylates of high batch-to-batch consistency and free of impurities like sodium that enter as a result of traditional methods of metathesis (double decomposition). The company's oil-



LONZA.
Development.

A-L

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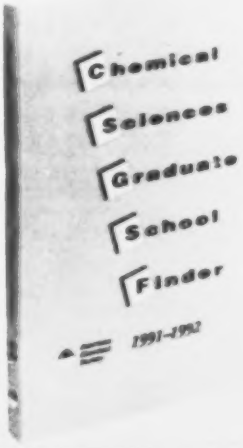

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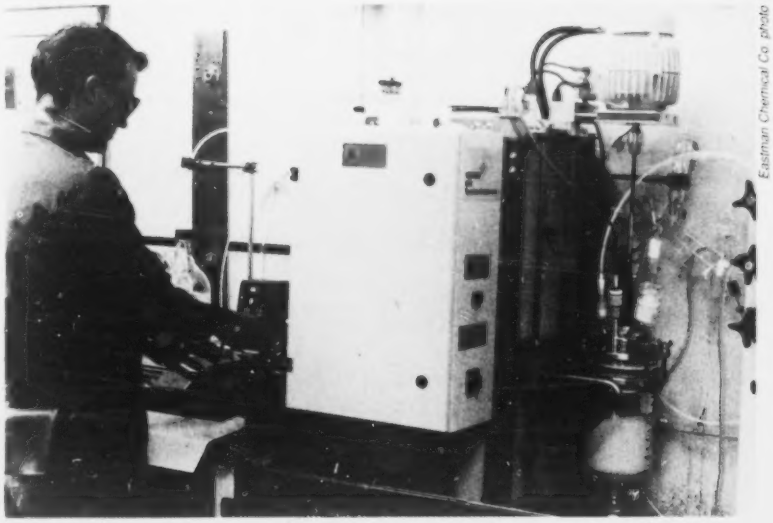
soluble or water-dispersible metal carboxylates find uses as coatings; rubber, plastics, and lubricant additives; and as homogeneous catalysts. They also are precursors of heterogeneous metal catalysts on mineral supports.

Affiliation with Outokumpu also brings technology to OM Group allowing it to make such inorganic salts as chlorides, nitrates, and sulfates, Tinker says. But more important than technology, the new firm offers technical support and reliability of supply of cobalt and nickel. The price and supply of these metals fluctuate frequently.

Sigma-Aldrich Corp., Milwaukee, bought Fluka Chemie of Buchs, Switzerland, and Ronkonkoma, N.Y., in 1989. Like Sigma-Aldrich, Fluka supplies laboratory reagent chemicals and bulk chemicals as catalog items or produced to order. The Milwaukee concern has set up a marketing organization called SAF to sell bulk chemicals and custom production services.

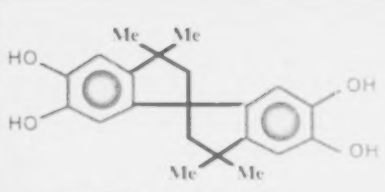
Clint Lane, executive vice president, says one forte of the company is production of enantiomeric compounds. These are available by asymmetric syntheses with *B*-chlorodiisopinocampheylborane or through resolutions of racemic mixtures. And the Sigma Chemical Co. subsidiary in St. Louis offers custom synthesis of biochemicals, mostly radiolabeled compounds.



Eastman Chemical Co. photo

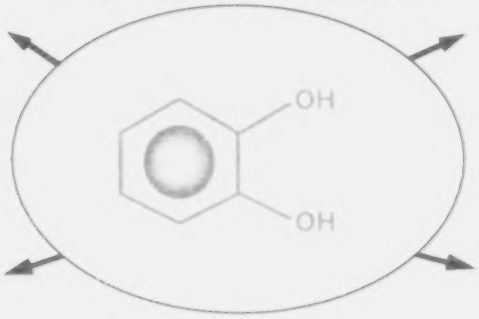
Technician runs design experiment prior to scaleup of a custom chemical project

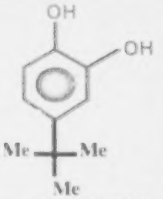
Another recent acquisition was SmithKline Beecham's fine chemicals plant in Conshohocken, Pa., by Lonza of Fairfield, N.J., in 1991. Raimund J. Miller, who is director of commercial development, says the new plant will expand Lonza's ability to offer custom production in the U.S., as will a



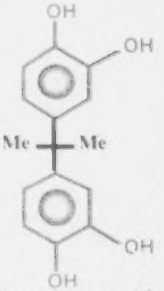
Photographic Image Stabilizer
JP 02286642 (1989)

CATECHOL
The Versatile Raw Material

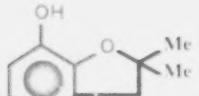




Polymerization Inhibitor
JP 02152939 (1990)



Thermal recording material
JP 02185491 (1989)



Agrochemical (insecticidal) intermediate
U.S. 4639536 (1987)

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planned expansion of the Lonza plant in Bayport, Tex.

Like so many firms successful in custom production, Lonza is skilled in handling dangerous substances. The company already makes diketene in Texas, and will bring its overseas technology for hydrogen cyanide and chlorosulfonyl isocyanate there as well. These chemistries are currently practiced at the plant of the parent company in Basle, Switzerland. There Lonza uses hydrogen cyanide to make malononitrile, which is used to produce triamterene to treat high blood pressure, and to make aminopyridines for herbicides. Chlorosulfonyl isocyanate is used to introduce carboxamide groups into drug molecules.

Indeed, syntheses involving diketene will have to be custom-ordered. Lonza and Eastman Chemical, the other producer, have decided to stop shipping the intermediate because of the potential for accident with the explosive, acid-sensitive material.

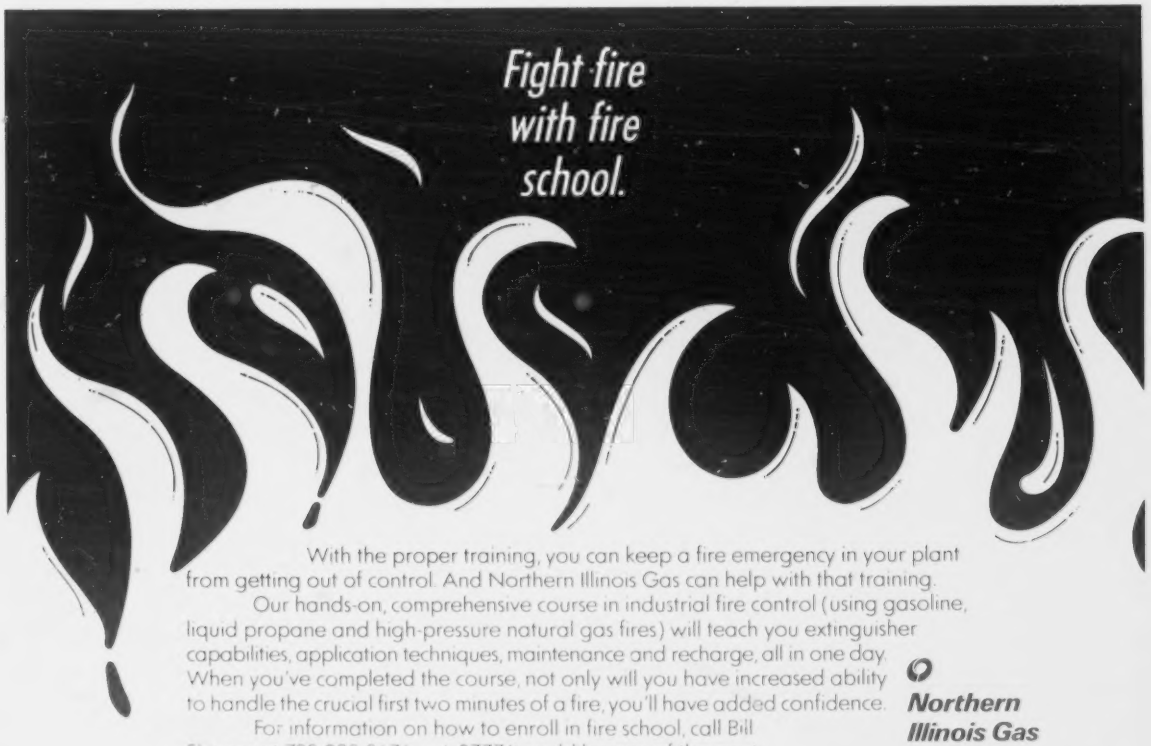
Another company with a European parent, Hüls America of Piscataway, N.J., also has garnered new custom production capabilities by acquisition. In 1987, the German parent bought the chemicals and plastics business of Dynamit Nobel; the acquisition resulted in the merger of Dynamit Nobel of America with the New Jersey firm. This merger spawned the organic chemicals producer Kay-Fries, and Petrarch, which makes organosilicon compounds.

The U.S. manager for custom production at Hüls America is Robert J. Morlino, who is vice president for intermediates and specialty chemicals. Whether the company fills a custom order from the U.S. or Germany depends on clients' desires and where the needed chemistries or equipment is avail-

Companies must balance efficiency of single-purpose equipment with flexibility of multipurpose equipment

	Single-purpose equipment		Multipurpose equipment
	Single product	Multiproduct	Multiproduct
Operation	Continuous	Continuous or batch	Batch
Advantage	Efficiency	Efficiency and some flexibility	Flexibility
Applications	Large-volume standard intermediates and bulk actives	Small-volume standard intermediates	Small-volume bulk actives and custom synthesis

Source: Arthur D. Little Inc.



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able. Morlino says he exchanges a monthly "sorry" list with his counterpart in Marl, Germany. This list describes queries that either person has had to decline in the past month but that the other may see as an opportunity.

In a change of direction elsewhere, Reilly Industries, Indianapolis, is moving away from custom manufacture, but bought Morflex of Greensboro, N.C., which does do custom manufacture. Acquired in 1990, Morflex offers a variety of chemistries and specializes in esters of polyfunctional acids. Though esterification may seem straightforward, Lee Skinkle, director of sales and marketing, says the firm's strength is in its ability to work with high, medium, and low molecular weight acids and alcohols and to process esters in liquid or solid form.

Like so many companies in custom production, Morflex has found a niche by doing some reactions but not others. The company does not do nitration or hydrogenation, for example, but has reliable sources to subcontract such chemistry. As Skinkle puts it, "The custom manufacturing industry is its own very important customer."

Just as Morflex has branched into other areas of custom production based on ester technology, so Pfanstiehl Laboratories, Waukegan, Ill., has capitalized on its expertise in sugar chemistry. Pfanstiehl president A. George Holstein says this capability has brought the company to the attention of customers wanting a custom supplier with a plant that is approved by FDA and that follows so-called good manufacturing practices. And the firm has applied techniques for sugar chemistry to such analogous problems as isolation of botanical products. In some of its work with sugars, Pfanstiehl makes the anticancer drug cytarabine, the 1-acetyl-2,3,5-tri-*O*-benzoyl-D-ribofuranose precursor to antiviral ribavirin, and the glucose-derived antipsoriasis agent amiprilose.

Custom synthesis has unique role in fine chemicals production

	Fine chemicals		
	Standard intermediate	Standard bulk actives[a]	Custom synthesis
Range of structures	Very broad	Very broad	Few
Applications of compounds	Several	Single	Single
Life cycle of compounds	Long	Short	Unpredictable
Basis of competition	Price	Price	Flexibility
Impact of raw material costs	High (> 60%)	Highly variable	Limited (< 40%)

a Generic drugs, pesticides, and electronic chemicals. **Source:** Arthur D. Little Inc.

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Another company with a differentiating specialty is Sepracor, Marlborough, Mass. Steve Brandt, director of marketing, says his firm custom-produces enantiomeric compounds by diastereoisomeric fractional crystallization, biocatalytic kinetic resolution, and asymmetric synthesis.

Diastereoisomeric resolution is the classical method that makes use of salts of racemic acids with, for example, enantiomeric α-phenylethylamine or racemic bases with enantiomeric tartaric acid, which are fractionally crystallized to resolve the substrate.

In biocatalytic kinetic resolution, an enzyme preferentially hydrolyzes one enantiomeric ester or amide in a racemic mixture. Sepracor has devised hollow-fiber membrane bioreactors for kinetic resolution in which the membrane material bears an immobilized enzyme.

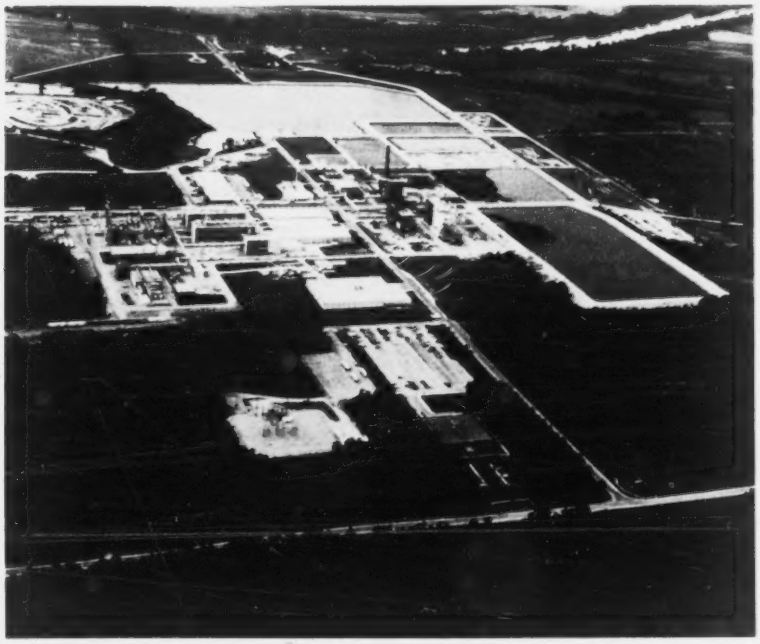
In one version, an organic solution of racemic glycidyl butyrate flows along one side of a membrane bearing immobilized pig pancreatic lipase. An aqueous phase flows along the other. The lipase hydrolyzes (*R*)-glycidyl butyrate preferentially. (*R*)-Glycidyl alcohol passes through the membrane and is carried away for collection in the aqueous phase. Brandt says that potential production in the company's commercial-scale modules is 100,000 kg per year.

For asymmetric syntheses, Sepracor has licensed the catalytic asymmetric dihydroxylation of olefins developed by organic chemistry professor K. Barry Sharpless, who is now at Scripps Clinic Research Institute, La Jolla, Calif. (C&EN, July 22, 1991, page 19).

For some types of expertise, U.S. clients for custom chemical production have found it not only possible but necessary to go overseas. For example, Lonza's Miller says his firm specializes in ozonolysis at its plant in Basle, Switzerland. Few companies do ozonolysis in the U.S.

Mary Collins, manager of process development at Newport Pharmaceuticals Ireland in Dublin, described her company's facilities for carrying out reactions down to −100 °C to the Chemical Specialties buyer-supplier symposium in Cherry Hill, N.J., last October. The advantages of very low temperatures are reaction selectivity and stereoselectivity in asymmetric syntheses, Collins said.

The low-temperature reactor at



Eastman Chemical's custom chemical facility in Batesville, Ark.

What custom production entails

Custom chemical production is the synthesis of organic or inorganic compounds according to a buyer's special order. These compounds may be intermediates that are unavailable from the catalogs of any company in the fine chemicals industry (standard intermediates). Or they may be finished end products originally discovered in customers' research (bulk actives). Other aspects of the total custom chemical manufacturing industry include such physical processes as drying, grinding, or distillation.

A subset of custom production is toll manufacture. This occurs when a customer ships a raw material to the

Newport is chilled by circulating methanol, which is brought to the proper temperature by circulation with liquid nitrogen through a heat exchanger. In one synthesis the company does, a re-

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custom producer to carry out one or more synthetic steps before getting the product back.

Some companies order custom production because they have no spare pilot plant or large-scale capacity of their own. Many firms wait until a product is a proven marketing success before building capacity for it. And in the current recession, companies that might otherwise build or expand their own capacity postpone investment until better times.

Custom production is also ordered when it involves unfamiliar chemistry—for example, synthesis of an inorganic catalyst for the process of an organic chemicals producer. Dangerous reactions such as nitration, high-pressure hydrogenation, or phosgenation might be farmed out, especially by firms whose own plants are in populated areas.

Analyst Enrico Polastro of Arthur D. Little International, Brussels, outlined the characteristics of chemical production within the fine chemicals industry in a presentation to the Chemical Specialties convention last October in Cherry Hill, N.J.

First, he said, custom chemicals have an unpredictable life cycle. This is because a client's product may fail in the market, a drug may show toxic side effects, or a customer may take production in-house. And a custom compound has only one use—that of the customer—compared with standard intermediates that are precursors to several compounds.

Second, in contrast to standard intermediates or bulk actives, delivered price plays a small role in whether the custom producer gets the business. Custom producers compete on the basis of flexibility and rapidity of response.

Third, because most of custom production cost is in process development and time in special equipment, raw materials cost is less than 40% of delivered price, compared with more than 60% for standard intermediates or bulk actives.

actant must be added over a period of 10 hours to a stainless steel reactor chilled precisely to -65 C the whole time.

Collins estimated this step adds $1850 per kg-mole to the cost of the final product, which would be $12.33 per kg for a molecular weight of 150. This cost may seem high, yet the same reaction carried out conventionally at 0 C would produce only half the yield, require much longer workup time, and have to be carried out in a glass-lined vessel.

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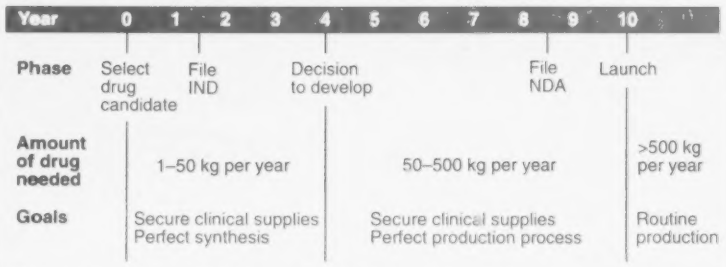

IND = Investigational new drug. NDA = New drug application. **Source:** Hoffmann-La Roche

ranged when customer and custom producer meet, is most often arranged through the client's purchasing agent, says Morlino of Hüls America. His experiences are probably representative of custom producers meeting business prospects.

Purchasing agents for custom production customers are usually associated with research, specialize in buying custom production, and have degrees in chemistry, as do Hüls' salespeople. Typically, salespeople want to expand their contacts by getting beyond the purchasing agent to persons in research or production. And also typically, purchasing agents don't want to allow this. They fear losing control of orderly contracting. And the purchasing agent may be the only one who knows what information may be given to the prospective vendor.

Like so many vendor companies that have expanded by acquisition, Hüls tries to keep a small-company atmosphere and avoid bureaucracy. This is hard, Morlino says, because increasingly stringent regulations on safety, pollution, and waste disposal require centralized management. In addition, customers now often ask to see that Hüls has written policies and procedures and follows these.

Part of avoiding bureaucracy is the ability to sign secrecy agreements quickly. Morlino says Hüls has streamlined this legal process, and that secrecy agreements are easier now. He recalls that 10 years ago, a customer might demand in the agreement that the vendor return any paperwork associated with the contract on demand. But after much paperwork over many years, it might be impossible to guarantee complete compliance.

Also like other vendors, Hüls takes the risk that the customer's end prod-

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CIRCLE 37 ON READER SERVICE CARD

Conventions key to custom chemical producers

Two conventions have become established in the U.S. to introduce buyers of custom chemical production to services and firms that might supply them. The seventh annual meeting of Informex will be in New Orleans, from Feb. 17 to 19. And the third annual meeting of Chemical Specialties symposium and exposition will take place from Oct. 5 to 8 in Cherry Hill, N.J.

Informex, which is sponsored by the Synthetic Organic Chemical Manufacturers Association (SOCMA), is the only convention solely dedicated to concerns of custom production. The meeting will begin on a Monday at the Fairmont Hotel with registration and an evening reception. The several hundred attendees who are expected will have the next two days to tour an exposition of about 120 firms that offer custom chemical synthesis and/or physical processing.

In addition, Tuesday will feature panel discussions on environmental and waste disposal issues, plus a plenary paper by analyst Ernest Gilmont of Arthur D. Little Inc. on competitive intelligence. Moderated by Cable Network News reporter Marc Levinson, the environmental issues panel will include actor and environmental activist Ed Begley Jr., and Rob McCord of the Congressional Institute of the Future. The waste disposal issues panel will consist of Art Gillen of BASF Corp., Jim Norris of BCM Engineering, and Jim Bratina of Reilly Industries.

uct may fail, or that it will succeed and the customer will take production in-house. In such a case, the vendor may lose all the money spent on process development after delivery of only a small amount of product.

Morlino acknowledges that most custom production contracts are worthless, because the customer will ask to be let out according to business exigencies. And Hüls may agree to cancellation to keep up a long-term relationship. Contracts exist, then, mostly to please managements.

If this is the way things often appear to a vendor, John W. Scott described one customer's view to the Chemical Specialties symposium in October. Scott is director of chemical development at Hoffmann-La Roche, Nutley,

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Chemical Specialties USA '92, which is organized by Spring Innovations of Stockport, England, is more generally concerned with specialty chemicals, but includes papers and exhibits dealing with custom production. This meeting also will begin with registration late on a Monday, at the Hyatt Cherry Hill Hotel. About 1000 persons are expected to register. The affair will consist of a symposium, an exposition, and sessions of meet-the-supplier seminars called Specmart.

The symposium program has not yet been finalized, but plans call for it to begin on Tuesday with about 20 papers spread out over two mornings and an afternoon. Speakers will represent custom chemical service firms, their clients, and consultants who follow this segment of industry.

The exposition opens Wednesday and will run two full days. About 100 exhibitors are expected. On Wednesday afternoon and Thursday morning, attendees can drop in on small Specmart seminars by selected supplier firms.

Those interested in attending Informex should contact Amanda Frederick of SOCMA, 1330 Connecticut Ave., N.W., Suite 300, Washington, D.C. 20036, fax (202) 659-1699.

Those in North America who wish to attend Chemical Specialties USA '92 should contact the U.S. representative, Brandon Associates, P.O. Box 1244, Merrimack, N.H. 03054, telephone and fax (603) 424-2035.

N.J. Fine chemicals companies that want to supply Roche must deal with greater complexity of synthesis, increasing attention to FDA for validation and statistical process control of production, and Roche's constant striving to improve quality.

As to complexity, Scott notes that new drugs under development at his firm require 12 to 23 chemical steps. For those that are chiral, Roche has adopted a policy of developing only one enantiomer, which adds to complexity. Overall yields of active bulk compounds can be less than 5%. Because Roche is located in a densely populated New York suburb, vendor firms have the opportunity to supply the company with custom production based on dangerous reactions and reactants.

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As to FDA's closer attention to processes, suppliers will have to work with Roche in thorough studies of each chemical step and put the steps under statistical process control. And suppliers to Roche must upgrade quality to Roche's own standards in order to eliminate problems in processes that involve rework even after commercial production has begun.

As Roche's drugs move through development, amounts needed increase and production philosophy changes. For the first four years after selection of a drug candidate, annual needs are only 1 to 50 kg. The emphasis is on getting enough for clinical studies with little attention paid to synthesis or costs.

About the fourth year, the firm decides on full development. At this moment, needs rise to from 50 to 500 kg per year, and emphasis changes from synthesis to process. As to potential suppliers to Roche, Scott distinguishes among "kilo labs," fine chemicals manufacturers, and other drug firms.

Directories help buyers locate sellers

People seeking custom chemical production can find providers of such services in several published sources. The Custom Chemicals Directory section of the American Chemical Society's "Chemcyclopedia" lists providers alphabetically with addresses, telephone numbers, and capsule summaries of the expertise of each. The current 1992 edition costs $60.

Brandon Associates, Merrimack, N.H., publishes "The Brandon Guide to Custom Chemical Synthesis Services—North America" at $170 for the 1991 edition. The price includes two semiannual updates. The book gives one-page entries for more than 300 firms, cross-indexed according to 200 processes. The one-page entries include equipment and processes available, details of pollution control, waste handling, and analytical instruments, and whether the plant is approved by the Food & Drug Administration.

Custom Guide Co., Closter, N.J., puts out a "Custom Processing Services Guide" at $300 for the 1990 edition, including two semiannual updates. The book gives one-page entries for almost 400 companies, listed by plant locations and cross-indexed according to processes. The format is designed for users without purchasing agent experience, who can compile a list according to capabilities and then limit it to those plants nearby for visits. The one-page entries include equipment and processes available.

Delphi Marketing Services, New York, N.Y., will publish the 1992 edition of its "Directory of Custom Chemical Manufacturers" in February, priced at $260. The one-page entries for almost 300 firms include equipment, unit operations, and reactions available, whether there is general and product liability insurance and a person designated for regulatory affairs,

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and whether the plant is FDA-approved.

Also in February, Quest Data, Nashville, Tenn., will put out a new edition of "A Guide to Custom Chemical Manufacturing & Processing"; the group expects to price the publication at about $150. Three semiannual updates are included in the price. More than 500 companies are listed. In addition to equipment and processes available, a full slate of chemicals regularly produced is given. Entries include provisions for pollution control and waste disposal, analytical instruments available, and whether the plant is FDA-approved.

For buyers of custom chemical production who don't want to pore over directories or keep up their own files, brokers provide an attractive alternative. One such broker is Jonas Chemical Corp., Brooklyn, N.Y. Jonas doesn't produce any custom chemicals itself but can suggest where to get things done.

Kilo labs are small companies that generally produce in 22-L glass flasks. Though their flexibility is good and their staff quality high, they are not large enough to carry out the type of development program needed in the new industrial climate.

Other drug companies and their wholly owned custom production subsidiaries are fully able to meet evolving requirements for development and are thus potential suppliers to Roche. But there are worries in cases where the other drug company has drugs in classes similar to those of Roche. That leaves the larger fine chemicals suppliers, who will reap tremendous opportunities provided they can keep adjusting to evolving requirements.

Although drug companies are the largest dollar market for custom chemical production, chemical and plastics companies buy the most diverse kinds of products. At Dow's Michigan division, Joseph Raab is a purchasing agent for chemical raw materials. And at Monsanto Chemical Co., Edward Moore is manager of toll manufacture and custom synthesis. Both are longtime veterans of research and production at their companies, each with 15 years in purchasing alone.

In his constant search for potential suppliers of custom production, Dow's Raab uses SRI International's "Directo-

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ry of Chemical Producers," the CIS "Directory of World Chemical Producers," and Chem Sources. Scott maintains his own file of companies and finds that trade shows such as Informex are useful.

Moore of Monsanto keeps his own computerized file of suppliers, cross-indexed according to 20 kinds of equipment, 20 chemistries available, and geography. Such computer systems are available to buy, he says. Moore also makes contacts at Informex. Moore makes only limited use of brokers, whereas Raab uses them sometimes to find candidates that do not have their own sales organizations.

Both men are concerned that the custom suppliers have responsible approaches to safety and the environment. This is because both seek long-term relationships, uninterrupted by regulatory shutdowns or accidents, and want to avoid third-party liability. But, also as Raab puts it, "We want to be sure they have the same values as Dow." And Moore says, "We look at the vendor as a part of Monsanto."

In one anecdote about approaches to keeping long-term relationships, Raab says recently his company had to cancel a project that had been let out to three custom contractors. These contractors feared they would be "left holding the bag" on costs they had incurred. But Dow renegotiated expenses with them to "make them whole."

Each man has counterparts in other regions of the world who can order technologies there that are not widely available in the U.S. Raab notes that European firms are expert in ozonolysis, and Japanese companies are good with amino acid derivatives. □

Eastman Chemical Co. photo

Worker monitors custom chemical production at plant in Sterling, England

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